

## OBSERVATIONS

# Insulin-Sensitizing Effects of Telmisartan

Implications for treating insulin-resistant hypertension and cardiovascular disease

The angiotensin II type 1 receptor blocker (ARB) telmisartan was reported to activate the peroxisome proliferator-activated receptor- $\gamma$  (PPAR- $\gamma$ ) in transactivation assays, whereas other ARBs, with the possible exception of irbesartan, did not (1). Telmisartan also induced adipogenesis and increased the expression of PPAR- $\gamma$  target genes in preadipocyte fibroblasts (1), both of which are hallmark properties of PPAR- $\gamma$  agonists.

We report a case of a 52-year-old man with hypertension; visceral obesity (BMI 34.4 kg/m<sup>2</sup>), and impaired glucose tolerance (pre-diabetes), in whom administration of telmisartan (80 mg/day) normalized blood pressure, improved insulin resistance, and reduced plasma triglycerides. During the 10 weeks after initiating telmisartan, his fasting blood glucose (6.83 mmol/l) and insulin (30  $\mu$ U/ml) levels progressively decreased to 5.78 mmol/l and 15  $\mu$ U/ml, respectively, corresponding to a 58% decrease (9.11 to 3.85) in the homeostasis model assessment of insulin resistance score, an index of insulin resistance (2) calculated as [insulin (microunits per milliliter)  $\times$  glucose (millimoles per liter)]/22.5. Fasting triglycerides were decreased by 21% (1.54 to 1.21 mmol/l).

At week 10, he was switched to a therapeutically equivalent dose of valsartan (160 mg/day), a less expensive ARB on his health maintenance organization formulary, which did not activate PPAR- $\gamma$  in vitro (1). After 5 weeks on valsartan (week 15), his homeostasis model assessment of insulin resistance score increased by 55% to 5.98 (blood glucose 6.12 mmol/l and insulin 22  $\mu$ U/ml) and triglycerides increased by 30% (to 1.57 mmol/l), reversing the improvements in insulin

sensitivity and triglycerides obtained with telmisartan. Valsartan was discontinued when he was permitted to restart telmisartan. Over the following 4 weeks, his homeostasis model assessment of insulin resistance score again decreased by 16% to 5.02 (blood glucose 5.94 mmol/l and insulin 19  $\mu$ U/ml), as insulin sensitivity improved and triglycerides also improved (decreased to 1.40 mmol/l). Throughout the observation period, body weight, total cholesterol, and HDL and LDL cholesterol remained unchanged (data not shown).

This patient's insulin resistance and triglycerides improved on telmisartan, but deteriorated while on valsartan, an ARB that does not activate PPAR- $\gamma$  (1), implying that telmisartan may have insulin-sensitizing and triglyceride-lowering effects related to its ability to activate PPAR- $\gamma$ . However, more clinical cases are needed to draw a definite conclusion.

The widely prescribed antidiabetic PPAR- $\gamma$  agonists, rosiglitazone and pioglitazone, are limited by their propensity to provoke fluid retention, peripheral edema, and heart failure, particularly in patients also taking insulin (3). However, telmisartan does not promote edema or heart failure and might in fact counteract the fluid retention associated with PPAR- $\gamma$  activation by virtue of its ability to block angiotensin II type 1 receptors in the kidney (4).

These findings may provide a new basis for drug choice in insulin resistance and hypertension and should motivate systematic studies on the therapeutic effects of telmisartan in patients with insulin resistance and related metabolic and cardiovascular diseases. ARBs that activate PPAR- $\gamma$  might exert beneficial effects on carbohydrate and lipid metabolism that could promote improved cardiovascular outcomes (4,5).

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## Passing the Torch at the International Diabetes Federation

At the triennial International Diabetes Federation (IDF) Congress in Paris this past August, Sir Professor George Alberti completed a distinguished 3-year term as IDF president. George's contributions to the fight against diabetes have been many during a distinguished career spanning more than three decades. From his work pioneering the use of "low-dose" insulin in the treatment of diabetic ketoacidosis to his numerous insightful studies of insulin's metabolic actions in healthy and diabetic humans, he has been a bright intellectual light. However, his scientific contributions have if anything been surpassed by his work as a "world citizen." Whether establishing joint initi-